PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	A Retrospective Cross-Sectional Analysis of the Changes in Marijuana Use in the United States, 2005-2018
AUTHORS	Mitchell, William; Bhatia, Roma; Zebardast, Nazlee

VERSION 1 – REVIEW

REVIEWER	Mallie J. Paschall Pacific Institute for Research and Evaluation
REVIEW RETURNED	25-Mar-2020

GENERAL COMMENTS	This study used NHANES data to assess trends in marijuana use among demographic subgroups in the U.S. from 2005 to 2016. Results indicate increases in the prevalence of past-year marijuana use among older adults, females, and adults with at least a high school education. Higher rates of recent use were observed for younger adults, males, and adults with income below poverty-level. No significant changes were observed for lifetime marijuana use and age of first marijuana use. These findings provide useful information regarding possible effects of marijuana legalization in the U.S. The authors refer to past-year marijuana use as "recent use." This is questionable since recent use is typically defined as past-month or past-week use, so I would recommend just using past-year marijuana use. The title of Table 1 includes cocaine, heroin, and methamphetamine use. Is this a typo? If not then the results are not just about marijuana use and the title and focus of the paper should be revised. It's not clear why the multivariate analyses in Table 3 do not include year and possibly also interaction terms reflecting subgroup differences in trends in past-year marijuana use. Additionally, the authors may want to consider including an indicator of the number of states that have legalized medical/recreational marijuana each year to capture effects of legalization on past-year use.

REVIEWER	Michelle Rotermann Statistics Canada – Canada
REVIEW RETURNED	31-Mar-2020

GENERAL COMMENTS	**Review –Demographic changes in the prevalence of marijuana use in the United States, 2005 to 2016** Thanks very much for the opportunity to review this manuscript. I would also like to apologize for my significant delay in completing it due to unprecedented

circumstances related to Covid-19.

My overall assessment of the paper is that it requires major revision in order to help the paper achieve its stated objectives and bring the manuscript up to a level deserving of publication. My assessment suggests work is needed in most sections of the paper.

The paper uses six waves of NHANES data to examine overall trends in marijuana use (past year, lifetime, and age of initiation) in the United States and then examines sociodemographic factors associated with past year marijuana use using simple descriptive statistics and odds ratios. Additionally, it is stated that there is an exploration of recent literature regarding the cost-effectiveness of medical and social marijuana legalization. But in the absence of data this discussion item is of limited value (although some themes have the potential to be reworked and included in the Introduction as part of the rationale for why marijuana use is deserving of study).

In summary, the paper does examine self-reported marijuana use in the USA using 6 waves of NHANES data from 2005/06 to 2015/16 but the paper does not make a sufficiently convincing argument for why the paper is needed, how the variables (outcomes or covariates were selected) why the analytical approach is appropriate, how one part of the analysis relates to another, etc. Some part of the analysis lack focus. Additionally, content more appropriate for one section (such as Methods or Limitations) is oftentimes found in another (e.g. Results or Discussion). Important limitations are also missing and the data presented does not include the most recent available: i.e. excludes 2017/2018.

To help the authors I have provided some examples leading to my "No" answers on the review form:

1) Are the methods described sufficiently to allow the study to be repeated? No.

   a. pg 6/ln 22- not clear from this section if 95% confidence intervals were bootstrapped, Taylor linearization or jack-knife variance estimated to account for the complex survey design of NHANES. What would be the impact on study findings if complex survey design not taken into account?
   b. pg 6- recommend adding a similarly worded statement: Results at the $p < 0.05$ level were considered statistically significant. If this is true; adjust accordingly if not.
   c. Notes associated with Tables 1-3 state the results were age-standardized. Methods section Pg 6 does not mention age-standardization. Clarify/correct.

2) Are the results presented clearly? No.

   a. pg 6/ln 41 – number of respondents in study is not a finding (suggest moving to Methods section); recommend adding the number of survey respondents included in the study.
   b. pg 6/ln 43-45 –presentation of extent of missing data seems to be out of place. Either include as part of Methods or include as limitation. These are not your main results.
   c. Table 1: title includes cocaine/ heroin/meth…please clarify/correct.
   d. Table 1 – correct/clarify title. Follow example from e.
   e. Unclear if this is specific to the journal but it might be preferable to include the target population covered by the survey in the titles of each of the data tables and include the data source as part of the
   Key. E.g. suggest renaming tables: Table 2: Prevalence of self-reported past-year marijuana use among non-institutionalized Americans aged 18 to 69, by selected demographic factors 2005/2006 to 2015/2016. Table 3: also

suggest changing the title. Adjusted odds of past-year marijuana use among non-institutionalized Americans aged 18 to 69, 2005/2006 to 2015/2016.

3)   If statistics are used are they appropriate and described fully? No.

   a. pg 6/ln 26: please provide rationale for opting for chi-square tests as compared to t-testing in Table 2. If t-testing was used and the reference categories from the multivariate analysis presented in Table 3 were applied to Table 2 the approach would provide a logical link between the Tables and would yield additional information. In particular, one would learn whether bivariate differences from Table 2 persisted even when other factors were also taken into account (Table 3).
   b. pg 7/ln 11: Bivariate descriptive analysis conducted using each wave separately indicated that the pattern for each variable were not always consistent. When the 6 waves of data were combined are there any disadvantages? How were differences across years taken into account? Was there a wave (year) variable included in the logistic regression model?

4)   Are the discussion and conclusions justified by the results? No.

   a. pg 7/Ln 36 The discussion item about Native Americans, urban/rural and/or western states is interesting but with sentence concluding with "these demographic factors not included in our analyses" is insufficient. If possible, please include a statement about how variables (outcomes and demographics) studied were selected.   If variables like Native American identifiers are not available state this or maybe they were not measured consistently across the data years then this information could be included as part of the limitations section.

   b. pg 7/Ln 40 Unclear how the authors concluded that the characteristics of medical marijuana users altogether different? The reason for using marijuana was not presented in this analysis and while it is true that other research has found differences between medical and non-medical users this statement seems out of place given the data presented. Suggest deleting.

   c. pg 7 –discussion around medical and recreational seems better suited to limitations section as the analysis presented neither distinguishes medical from recreational users nor persons living in states with medical marijuana access and/or legal recreational access. Suggest simplifying and/or moving to limitations.

   d. pg 7/8 –discussion item around changing trends in use among adolescents also seems disconnected from study results and/or target population of the study. According to Table 2 – prevalence rates of past year marijuana use among 18-29 stable although it seems the authors missed this comparison. Another point which could be included in the limitations section is that youth aged 17 or younger were not included in this study. Because important segments of adolescents are not included in this study suggest simplifying the paragraph about youth use. On the other hand, authors could highlight the increasing use among 50-69 year olds and indicate that the NHANES results echo the results found by Salas-Wright.

   e. pg 8 – discussion about trends in use not restricted to states with changing legalization. This study does not take into account the state of the respondent

or when each state passed legislation or established marijuana for commercial sale. For me this is content for the limitations section and not a discussion item. The authors could counter this limitation by stating that increasing trends of marijuana use appears not to be restricted to states with changing legalization.

f. pg 8 – the authors state that tobacco smoking is a significant risk factor for marijuana use. This variable is available in NHANES (from what I understand). Understanding why these variables were excluded from this study is important information. A similar explanation as to why the use of other drugs and non-medical use of prescription medication was also not included. This material could be included in the limitations section.

g. pg 8 –a secondary objective of the paper was stated to explore the economic and societal cost-effectiveness of marijuana legalization. However, data are not presented and instead this section is disconnected from the analysis of changing prevalence rates and sociographic factors associated with an increased likelihood of being a past-year marijuana user. In its current form suggest removing. However, some points such as legalization leading to lower marijuana prices could be offered as factors leading to increasing prevalence.

h. pg 8 – discussion about social justice could be dropped.

5) Are the study limitations discussed adequately? No.

   a. According to pg 5/Intro: marijuana use is legal by adults aged 21 or older but the paper looks at marijuana use among 18 to 69 year olds. Please include the rationale for including 18-20 year olds in study population. This might be as simple as stating that liberalizing medical or non-medical access has been correlated with decreases in perception of risk which in turn might lead to increased use and/or reported use.
   b. Changes in the willingness to report marijuana use could have affected your trend analysis. What might the impact be on your analysis? Are all sociodemographic groups likely to be affected similarly? There is a literature about social desirability which suggests what is socially desirable is varies by SES. Could this be affecting your results?
   c. NHANES, as a direct measures survey which uses a MEC prioritizes direct measures of health such as oral health, fitness measures, measured height and weight etc. Because respondents are requested to come to the MEC for some testing this means there are fewer collection sites (geographies represented) than would otherwise be the case with other drug use monitoring surveys such as NSDUH. Across the six waves of data used were there differences in the proportion of sample coming from states who had legalized access (either medical or recreational)? Are you able to provide a list of states (locations) by wave? This is a challenge of doing a secondary analysis (sometimes not all variables of interest are not available). Are NHANES data designed to produce national-level estimates? If so, are they appropriate for studying change when the change of interest is on-going and occurring at the state-level? An important part of conducting an analysis is selecting an appropriate data source. Are NHANES data appropriate? Statement could be added to Methods section; if challenges revealed (or cautions) these could be included in Limitations.
   d. There are several sources of marijuana use data in the US and understanding how different data sources compare is important. This may be an important limitation. Else, comparisons to other

papers/reports based on these other data sources could be included in the Discussion and similarities/differences acknowledged/stated even in light of the differences in coverage, mode of collection, question wording, study population, etc..

     e. Analyzing past-year prevalence rates is often regarded as necessary but insufficient indicator of the impacts of changing marijuana legislation on rates of use. A review of the NHANES website suggests other marijuana use variables are available in enough waves to allow for an analysis of changing intensities of use. The rationale for selecting the study's outcomes should be included in the Methods and their associated drawbacks, e.g. changing rates of use do not provide information about changes in intensity of use which could in turn affect rates of problematic use/substance use disorder.

Additionally, I have listed other questions or comments that did not map to the review form but nonetheless deserve some consideration:

i. According to the NHANES website 2017-2018 data are now available and because one of the main objectives is to examine trends in marijuana use over time having the most current data is important and feel the paper would be far more useful if the most recent data were included. An added benefit of including more up-to-date data would help strengthen the case that the paper is making a real contribution to the literature; including data from 2015 and before weakens this case.

    a. pg 4/Article summary- the article notes that it is the most recent study of trends of marijuana use. A quick search on the SAMHSA website suggests that there are other similar US-based analyses: E.g.

https://www.samhsa.gov/data/taxonomy/term/435 - https://www.samhsa.gov/data/sites/default/files/NSDUH-FFR1-2015Rev1/NSDUH-FFR1-2015Rev1/NSDUH-FFR1-2015Rev1/NSDUH-National%20Findings-REVISED-2015.pdf; https://www.samhsa.gov/data/sites/default/files/reports/rpt23237/NSDUHsaeLongTermCHG2018/NSDUHsaeLongTermCHG2018.pdf

ii. pg 5/Ln 9 – because the paper uses data which pertain to marijuana use in 2015/2016 (at the latest) sentences which reference "now" as opposed to a date range can be confusing. If more recent data are used then the alignment of the date ranges would also be minimized.

Misc. e.g. awkward sentences, potential inaccuracies or other:

pg 3/ln 23 – suggest replacing term recent use with use in the past year

pg 3/ln 39: While recent use was remained commonest…; revise

pg 3/ln 42-43: With high legalization adoption during…; revise. Perhaps reword: The data suggest that reported rates of marijuana use have been increasing at the same time as the number of states who have legalized the use of marijuana for medical and/or not medical purposes has also increased?

pg 4/Article summary: unclear of the intended purpose of this section. If it is to provide key findings then the section could benefit from a re-write in order to highlight key findings e.g. prevalence rate of past year cannabis; if it has been increasing over time and socio-demographic characteristics which are most strongly correlated with marijuana use. Other

statements such as 'limited by reporter bias" or state-based legalization information not available would be more appropriate in Data and/or Methods section.

pg 5/ln 20 – unclear what methadone (reference 10) has to do with marijuana use.

pg 6/Ln 3- recommend adding links to questionnaire and NHANES methodology reports

pg 6 –recommend adding cycle response rates.

pg 6/Ln 51 –unclear how "overall 18.8%" was calculated. Clarify/add to data table.

pg 6/Ln 58-how was recent marijuana use was higher determined? We can see that the 95% CIs do not overlap but this was not stated as part of the analytical approach. Similar question for income below poverty line (Ln 59); non-Hispanic black (pg 7/Ln 3), etc. Using reference categories and t-tests would enable statistical testing across groups.

REVIEWER	Patrick Janulis
	Northwestern University, United States of America
REVIEW RETURNED	06-Apr-2020

GENERAL COMMENTS	The manuscript is well written and examines in important and timely question. I have two minor concerns noted below.
	1) The high level of missing data is mentioned (~27%) yet little information is provided explaining how missing data was handled, although it is mentioned appropriately as a limitation and in the article summary, which I commend the authors for including. The authors should more specifically describe how missing data was handled which I assume was listwise deletion. However, there are numerous modern techniques for handling missing data including data missing not at random as the manuscript suggests may be the case. Including such an analysis would overcome one of the strongest weaknesses of the current manuscript.
	2) The discussion section is oddly structured with two small paragraphs quickly reviewing the main findings of the manuscript and then four much more substantial paragraphs providing an overview of related literature. This structure does not enable to the reader to easily contextualize the current findings by understanding how they relate to existing literature. I would suggest that the authors restructure the discussion section to more prominently reflect on the current findings within the context of the accumulated knowledge on US marijuana use, rather than comprehensively reviewing the current state of this knowledge.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1 comments:

1. The authors refer to past-year marijuana use as "recent use." This is questionable since recent use is typically defined as past-month or past-week use, so I would recommend just using past-year marijuana use.

We thank the reviewer for the clarification, and agree that the term "past-year" use is more informative. As such, we have modified all statements to "past-year use".

2. The title of Table 1 includes cocaine, heroin, and methamphetamine use. Is this a typo? If not, then the results are not just about marijuana use and the title and focus of the paper should be revised.

We thank the reviewer for noting this, and have edited the title for table 1 as follows: "Prevalence of marijuana use in adults in the United States, NHANES 2005-2018"

3. It's not clear why the multivariate analyses in Table 3 do not include year and possibly also interaction terms reflecting subgroup differences in trends in past-year marijuana use. Additionally, the authors may want to consider including an indicator of the number of states that have legalized medical/recreational marijuana each year to capture effects of legalization on past-year use.

We initially utilized 14-year weights for the present analysis, which accounted for the population structure during the entire 14-year period. We had also run regression analyses with single-cycle (2-year weight) covariates, which did not substantially or significantly alter covariate point-estimates (O.R.) or p-values, and was not originally reported.

When including the 2017-2018 NHANES data, all results (excluding education level) in table 3 became significant.

The inclusion of a single-cycle 2-year covariate for 2005-2018 data similarly did not substantially or significantly change the values of the coefficients (point-estimates) or p-value. The single-cycle (2-year weight) covariate for time (linear) is now reported in table 3, as noted. The authors would like to thank the reviewer for this recommendation.

Reviewer 2 comments:

The authors wish to sincerely thank reviewer 2 for such a comprehensive review of our manuscript, for such detailed and organized responses, and particularly for noting the new 2017-18 NHANES data available. We believe we have addressed all points, as outlined:

1. Are the methods sufficiently described to allow the study to be repeated?

a) Not clear whether 95% confidence intervals were boot-strapped, Taylor linearization or jack-knife variance estimated to account for the complex survey design of NHANES. What would be the impact on study findings if complex survey design not considered?

The default method for reporting standard errors for our analysis was *Taylor Linearization.* Given the complexity of the survey design, Taylor Linearization was considered an appropriate method. This has been clarified in the manuscript, with tracked changes have marked (line 156).

b) State results at the p<0.05 level was considered statistically significant

Amended, "Methods" (line 160).

c) Table 1-3 notes suggest results for age were age-standardized, but this is not mentioned in the methods. Please clarify/correct.

Amended, "Methods" (line 128; line 156)

2. Are results presented clearly?

a) Number of respondents is not a finding (suggest moving to Methods section)

We thank the reviewer, and note that the total number of participants is more appropriately included in STROBE item 10 (Methods) than item 13 (Results). As such, we have moved the total participants to the Methods section (line 136).

b) Presentation of missing data seems out of place. Either include as part of methods, or as a limitation. These are not main results.

Please see response to 2(a), and methods (line 137). We have also included how missing values were handled here (line 139). Missing data was also included in the Strengths and Limitations paragraph of the manuscript (line 268).

c) Table 1: clarify cocaine/heroin/methamphetamine in title

Re-named: Prevalence of marijuana use in adults in the United States, NHANES 2005-2018

d) Table 1: correct/clarify title

Re-named: Prevalence of marijuana use in adults in the United States, NHANES 2005-2018

e) Suggest renaming tables to include target populations covered by the survey

Table 1: Prevalence of marijuana use in adults in the United States, NHANES 2005-2018

Table 2: Prevalence of self-reported past-year marijuana use in adults in the United Stated, by selected demographic factors, NHANES 2005-2018

Table 3: Adjusted odds of past-year marijuana use in adults in the United States, NHANES 2005-2018

3. If statistics are used, are they appropriate and described fully?

a) Pg 6/ln 26: please provide rationale for opting for chi-square tests as compared to t-testing in Table 2. If t-testing was used and the reference categories from the multivariate analysis presented in Table 3 were applied to Table 2 the approach would provide a logical link between the Tables and would yield additional information. In particular, one would learn whether bivariate differences from Table 2 persisted even when other factors were also considered (Table 3).

A chi-squared test was considered appropriate by authors, given the size of the populations and the fact that the dependent (outcome) variable was binary (marijuana use yes/no) rather than continuous.

We have subsequently run t tests for all comparisons, which did not substantially change point-estimates or significance levels (reporting a t-statistic); and have reported chi-square analysis output in table 2. Table 3 uses a multivariable logistic regression model (z-statistic) to report odds ratios.

b) pg 7/ln 11: Bivariate descriptive analysis conducted using each wave separately indicated that the pattern for each variable were not always consistent. When the 6 waves of data were combined are there any disadvantages? How were differences across years considered? Was there a wave (year) variable included in the logistic regression model?

Please see response to reviewer 1, question 3.

4. Are the discussion and conclusions justified by the results?

a) pg 7/Ln 36 The discussion item about Native Americans, urban/rural and/or western states is interesting but with sentence concluding with "these demographic factors not included in our analyses" is insufficient. If possible, please include a statement about how variables (outcomes and demographics) studied were selected. If variables like Native American identifiers are not available state this or maybe they were not measured consistently across the data years then this information could be included as part of the limitations section.

We thank the reviewer for highlighting this, and have included more detail regarding why data was not analyzed in the main body of the Discussion (line 221), and in the Limitations section (line 272).

b) pg 7/Ln 40 Unclear how the authors concluded that the characteristics of medical marijuana users altogether different? The reason for using marijuana was not presented in this analysis and while it is true that other research has found differences between medical and non-medical users this statement seems out of place given the data presented. Suggest deleting.

We thank the reviewer for identifying this, and have deleted/modified the passage to outline that it was not explicitly studied here, but may (in part) explain the increased use among older populations (line 205).

c) pg 7 –discussion around medical and recreational seems better suited to limitations section as the analysis presented neither distinguishes medical from recreational users nor persons living in states with medical marijuana access and/or legal recreational access. Suggest simplifying and/or moving to limitations.

See point above (line 205); also included in Limitations (line 274).

d) pg 7/8 –discussion item around changing trends in use among adolescents also seems disconnected from study results and/or target population of the study. According to Table 2 – prevalence rates of past year marijuana use among 18-29 stable although it seems the authors missed this comparison. Another point which could be included in the limitations section is that youth aged 17 or younger were not included in this study. Because important segments of adolescents are not included in this study suggest simplifying the paragraph about youth use. On the other hand, authors could highlight the increasing use among 50-69-year-olds and indicate that the NHANES results echo the results found by Salas-Wright.

- Please note the re-structuring of the discussion section of the manuscript, to detail the new primary findings (with additional 2017-2018 data).
- Exclusion of younger age groups from the current study has been mentioned in the Discussion (line 214) included in the Limitations section (line 270).
- We have echoed the results found by Salas-Wright in our Discussion (line 203).

e) pg 8 – discussion about trends in use not restricted to states with changing legalization. This study does not consider the state of the respondent or when each state passed legislation or established marijuana for commercial sale. For me this is content for the limitations section and not a discussion item. The authors could counter this limitation by

stating that increasing trends of marijuana use appears not to be restricted to states with changing legalization.

We thank the reviewer for noting this, and for suggestions, which we have included. We have retained the paragraph discussion the importance of considering that trends in use are not restricted to states with legalization only (Discussion, line 236). We have outlined that we did not have linked geographical information with our questionnaire data in the Limitations section (line 273).

f) pg 8 – the authors state that tobacco smoking is a significant risk factor for marijuana use. This variable is available in NHANES (from what I understand). Understanding why these variables were excluded from this study is important information. A similar explanation as to why the use of other drugs and non-medical use of prescription medication was also not included. This material could be included in the limitations section.

Noted in Limitations, line 271.

g) pg 8 –a secondary objective of the paper was stated to explore the economic and societal cost-effectiveness of marijuana legalization. However, data are not presented and instead this section is disconnected from the analysis of changing prevalence rates and sociographic factors associated with an increased likelihood of being a past-year marijuana user. In its current form suggest removing. However, some points such as legalization leading to lower marijuana prices could be offered as factors leading to increasing prevalence.

As noted in response to reviewer 3: Although not directly analysed in the present study, we believe cost-effectiveness and social justice are important subjects related directly to our own findings, and worth discussion; they emphasize the importance of the present findings and contextualising where future research efforts could be directed (i.e. a cost-effectiveness analysis of legalisation).

h) pg 8 – discussion about social justice could be dropped.

As above: as noted in response to Reviewer 3: Although not directly analysed in the present study, we believe cost-effectiveness and social justice are important subjects related directly to our own findings, and worth discussion; they emphasize the importance of the present findings and contextualising where future research efforts could be directed (i.e. a cost-effectiveness analysis of legalisation).

5. Are the study limitations discussed adequately?

a) According to pg 5/Intro: marijuana use is legal by adults aged 21 or older but the paper looks at marijuana use among 18 to 69-year olds. Please include the rationale for including 18 to 20-year-olds in study population. This might be as simple as stating that liberalizing medical or non-medical access has been correlated with decreases in perception of risk which in turn might lead to increased use and/or reported use.

While recreational marijuana use is legal for adults aged 21 years and older, medical marijuana use is legal (in most US states with legalized medicinal use) for those aged 18 years and older. Because there was no distinction between whether marijuana was being used for medicinal or recreational purposes on the NHANES database, ages 18 and older were included in our analysis (to avoid not capturing those 18-21 who use marijuana for non-recreational purposes). Further, all data for adults aged over 18 years is publicly available on NHANES, so in order to maximize data available for our analysis (in light of higher volumes of data already missing), the entire adult cohort was used.

b) Changes in the willingness to report marijuana use could have affected your trend analysis. What might the impact be on your analysis? Are all sociodemographic groups likely to be

affected similarly? There is a literature about social desirability which suggests what is socially desirable is varies by SES. Could this be affecting your results?

The authors agree with the reviewer, and believe this would not have affected all demographic groups equally (as described in Methods (line 138)) and would have likely impacted our analysis (see Limitations, line 267).

c) NHANES, as a direct measures survey which uses a MEC prioritizes direct measures of health such as oral health, fitness measures, measured height and weight etc. Because respondents are requested to come to the MEC for some testing this means there are fewer collection sites (geographies represented) than would otherwise be the case with other drug use monitoring surveys such as NSDUH. Across the six waves of data used were there differences in the proportion of sample coming from states who had legalized access (either medical or recreational)? Are you able to provide a list of states (locations) by wave? This is a challenge of doing a secondary analysis (sometimes not all variables of interest are not available). Are NHANES data designed to produce national-level estimates? If so, are they appropriate for studying change when the change of interest is on-going and occurring at the state-level? An important part of conducting an analysis is selecting an appropriate data source. Are NHANES data appropriate? Statement could be added to Methods section; if challenges revealed (or cautions) these could be included in Limitations.

The authors agree that the NHANES data is limited in who is sampled. There are approximately 5,000 participants sampled biennially, with mobile study teams conducting interviews and examinations at different counties across the US each cycle. In an attempt to make data comparable to the US population, certain populations (i.e. older) are over-sampled, and weighted to represent the US population (Methods, line 131). Our dataset has also been age-standardized to represent the national population more accurately. However, details about whether states visited had legalization laws is not available in the NHANES dataset, which we agree is a limitation of most retrospective data analyses, using data not necessarily collected for the specific analysis in mind.

We have noted this in our Limitations section (line 273) of the manuscript.

d) There are several sources of marijuana use data in the US and understanding how different data sources compare is important. This may be an important limitation. Else, comparisons to other papers/reports based on these other data sources could be included in the Discussion and similarities/differences acknowledged/stated even in light of the differences in coverage, mode of collection, question wording, study population, etc.

The authors believe this is now better addressed in the Strengths and Limitations section of the manuscript (from line 266).

e) Analyzing past-year prevalence rates is often regarded as necessary but insufficient indicator of the impacts of changing marijuana legislation on rates of use. A review of the NHANES website suggests other marijuana use variables are available in enough waves to allow for an analysis of changing intensities of use. The rationale for selecting the study's outcomes should be included in the Methods and their associated drawbacks, e.g. changing rates of use do not provide information about changes in intensity of use which could in turn affect rates of problematic use/substance use disorder.

The rationale for choosing the questions for this analysis (ever-used, age <18 at first-use, and past-year use) was to minimize missing data.

While more quantitative questionnaire items did exist, the amount of missing data *far* exceeded the amount of missing data for the questions used in the present study (often >80% of data was missing).

For example, for the question "number of days used marijuana/month"; of 4572 responders, 3945 (86.3%) were recorded as "missing".

We have addressed limitations of retrospective, questionnaire, and self-reported data in the Strengths and Limitations section of the manuscript (line 267)

6. Additional comments to consider

a) According to the NHANES website 2017-2018 data are now available and because one of the main objectives is to examine trends in marijuana use over time having the most current data is important and feel the paper would be far more useful if the most recent data were included. An added benefit of including more up-to-date data would help strengthen the case that the paper is making a real contribution to the literature; including data from 2015 and before weakens this case.

2017-2018 NHANES data was released late February 2020, and the authors sincerely thank reviewer 2 for finding this. 2017-2018 data has now been included in all analyses.

b) pg 5/Ln 9 – because the paper uses data which pertain to marijuana use in 2015/2016 (at the latest) sentences which reference "now" as opposed to a date range can be confusing. If more recent data are used then the alignment of the date ranges would also be minimized.

"Now" is no longer a term used in the manuscript; rather "past-year use" and "most recent" findings, to avoid confusion between the presented results (which are now up till the end of 2018) and *current* findings.

c) pg 3/ln 23 – suggest replacing term recent use with use in the past year

All terms "recent-use" have been replaced with "past-year use".

d) pg 3/ln 39: While recent use was remained commonest...; revise

Revised: "While past-year use remained commonest" line 57.

e) pg 3/ln 42-43: With high legalization adoption during...; revise. Perhaps reword: The data suggest that reported rates of marijuana use have been increasing at the same time as the number of states who have legalized the use of marijuana for medical and/or not medical purposes has also increased?

Revised: "With high adoption of marijuana-legalization laws during this period, our results suggest an associated increase in past-year marijuana use" line 60.

f) pg 4/Article summary: unclear of the intended purpose of this section. If it is to provide key findings then the section could benefit from a re-write in order to highlight key findings e.g. prevalence rate of past year cannabis; if it has been increasing over time and socio-demographic characteristics which are most strongly correlated with marijuana use. Other statements such as 'limited by reporter bias' or state-based legalization information not available would be more appropriate in Data and/or Methods section.

Note, from BMJ Open instructions for authors for original research: "An Article Summary, placed after the abstract, consisting of the heading 'Strengths and limitations of this study', and containing up to five short bullet points, no longer than one sentence each, that relate specifically to the methods. They should not include the results of the study."

g) pg 5/ln 20 – unclear what methadone (reference 10) has to do with marijuana use.

We thank the reviewer for highlighting this, and have removed the Fingerhut reference (which had remained from an earlier draft of the Manuscript).

h) pg 6/Ln 3- recommend adding links to questionnaire and NHANES methodology reports

Data link is included in Data Statement: line 316.

i) pg 6 –recommend adding cycle response rates.

We have included the overall response rate in the form of missing data (32.9%, line 135). As there were unique response rates for each question, for each demographic, in each cycle, the authors felt it more appropriate to present an overall response rate (missing data), rather than the response rate for each question, in each cycle.

j) pg 6/Ln 58-how was recent marijuana use was higher determined? We can see that the 95% CIs do not overlap but this was not stated as part of the analytical approach. Similar question for income below poverty line (Ln 59); non-Hispanic black (pg 7/Ln 3), etc. Using reference categories and t-tests would enable statistical testing across groups.

The phrase "recent" has been changed to "past-year". The p-values in the far-right column of table 1 were calculated to demonstrate the significance of the trend of change seen in that row. We can see that only the "past year use" trend p-value is significant, and that the trend is increasing (working along the bottom (fifth) row from left to right).

Reviewer 3 comments:

1. The high level of missing data is mentioned (~27%) yet little information is provided explaining how missing data was handled, although it is mentioned appropriately as a limitation and in the article summary, which I commend the authors for including. The authors should more specifically describe how missing data was handled which I assume was listwise deletion. However, there are numerous modern techniques for handling missing data including data missing not at random as the manuscript suggests may be the case. Including such an analysis would overcome one of the strongest weaknesses of the current manuscript.

We thank the reviewer for outlining this, and have included further clarification in the methods describing how missing data was handled; "Missing data was handled by pairwise deletion to preserve data available for analysis" (line 139).

We have used pairwise deletion (rather than listwise deletion) to handle missing data, in order to maximise possible data available for analysis. Even when some participants had not responded to all "marijuana use" questions, those they did respond to were still preserved, for our analysis.

Given the inclusion of 2017-2018 data, the percentage of missing data has changed (32%), which we have noted. Given the size of the dataset, we believe this is still a considerable body of data to analyse, and have outlined limitations in drawing conclusions about marijuana use among older, female and <high school education populations, given high missing data.

2. The discussion section is oddly structured with two small paragraphs quickly reviewing the main findings of the manuscript and then four much more substantial paragraphs providing an

overview of related literature. This structure does not enable to the reader to easily contextualize the current findings by understanding how they relate to existing literature. I would suggest that the authors restructure the discussion section to more prominently reflect on the current findings within the context of the accumulated knowledge on US `marijuana use, rather than comprehensively reviewing the current state of this knowledge.

We agree with the reviewer's assessment of the structure of the discussion, and thank him for his suggested improvements. Accordingly, we have re-structured the discussion paragraph; to outline our two primary findings; (i) the demographic-specific increased past-year use, and (ii) the demographic-specific highest marijuana use. We have discussed how these findings compare to more recent US findings, and hope this reads more intuitively, now. See lines 193-223.

We have retained the three paragraphs thereafter in the discussion. Although not directly analysed in the present study, we believe they are important subjects related directly to our own findings; emphasising the importance of the present findings and contextualising where future research efforts could be directed (i.e. deeper understanding of risk factors for marijuana use after legalisation, changing use-patterns in states without marijuana legalisation, and a cost-effectiveness analysis of legalisation).

We hope that there is a clearer distinction in the discussion now, between our own findings and how they compare to similar US studies, and then the further salient points (outlined above).

VERSION 2 – REVIEW

REVIEWER	Mallie Paschall
	Pacific Institute for Research and Evaluation, USA
REVIEW RETURNED	16-May-2020

GENERAL COMMENTS	The authors have been responsive to reviewers' comments and have improved the manuscript. One key question was why the authors selected NHANES to assess changes in the prevalence of marijuana use versus other secondary data sources such as the National Household Survey on Drug Use and Health. A rationale for selecting NHANES should be provided in the Methods section.

VERSION 2 – AUTHOR RESPONSE

Reviewer 1 Comments:

The authors have been responsive to reviewers' comments and have improved the manuscript. One key question was why the authors selected NHANES to assess changes in the prevalence of marijuana use versus other secondary data sources such as the National Household Survey on Drug Use and Health. A rationale for selecting NHANES should be provided in the Methods section.

We thank the reviewer for outlining the importance of stating why NHANES is an ideal data source to use, rather than other secondary data sources. While we did not have access to other data sources, we also understand that NHANES is particularly well-suited to such an analysis. Because NHANES is biennially collected from different US counties, with multilingual, multidisciplinary healthcare teams and populations sampled to the represent age, gender and race of the general US population, NHANES is an idea source to demonstrate changes in a nationally-representative population of participants.

Please find the following changes, which we hope outline this clearly.

Line 126: Study teams consisting of multilingual physicians, medical and health technicians, and dietary health interviewers conduct interviews and perform examinations, and information collected is intended to be used to determine the prevalence of major diseases and risk factors for diseases, and for health promotion and disease prevention, making NHANES an ideal data source to describe marijuana use trends in a nationally-representative population.